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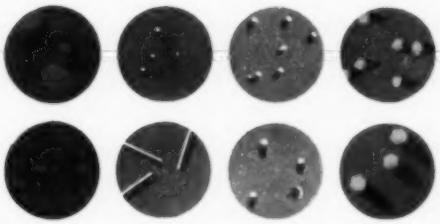

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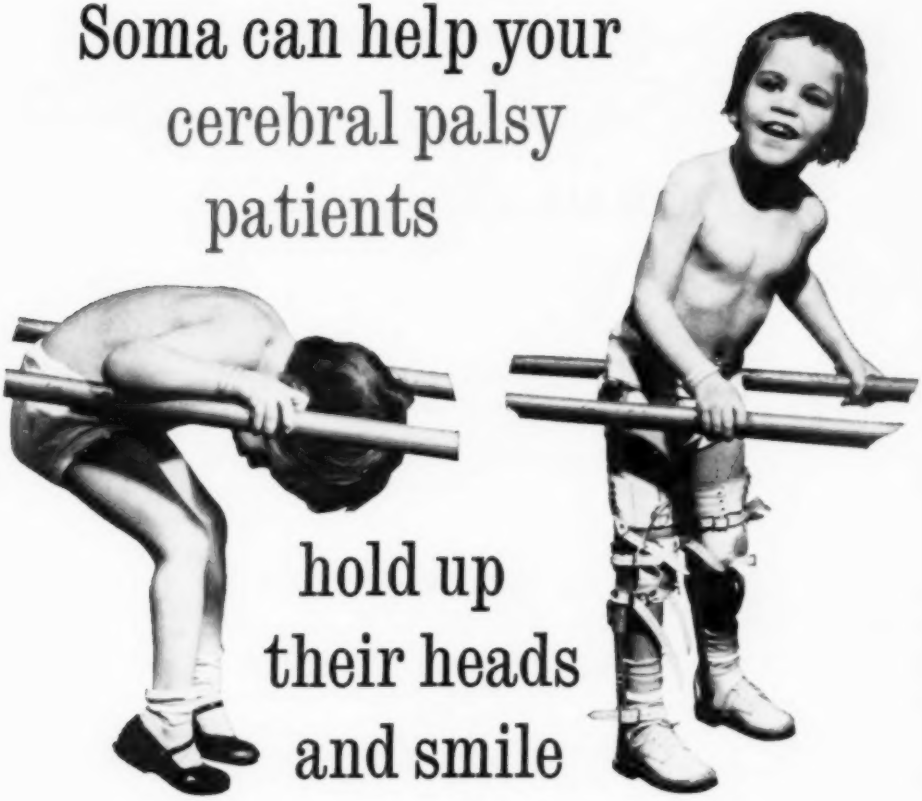

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Fundamental long-range studies on mental retardation, cerebral palsy and epilepsy, still relatively undeveloped areas in medicine, fall largely in the field of pediatric neurology. Hence, the new Laboratories, directed by Dr. Raymond D. Adams, Chief of Neurology, Massachusetts General Hospital and Bullard Professor of Neuropathology, Harvard Medical School, will bring together the research and clinical facilities headed by these Chiefs of Service: Dr. Nathan B. Talbot, Acting Chief of Children's Service, MGH, and Associate Professor of Pediatrics, Harvard Medical School; Dr. Erich Lindemann, Chief of Psychiatry, MGH, and Professor of Psychiatry, Harvard Medical School; Dr. James C. White, Chief of Neurosurgery, MGH, and Professor of Surgery, Harvard Medical School.

In keeping with the traditional teaching and research atmosphere which prevails at Massachusetts General, the new Laboratories will be dedicated to the challenge of finding answers to some of the most serious and least understood problems in medicine—diseases of the brain in infants and children. As infectious diseases are brought under control, the proportion of infants and children entering wards of general hospitals with diseases of the nervous system, is undergoing steady increase. State schools for mentally retarded children are filled to capacity with those who have suffered irrevocable effects of neurological disease. The United States Public Health Service is beginning to support several training centers, and the American Academy of Neurology now recognizes pediatric neurology as a sub-specialty. Yet, such efforts are small when considering the magnitude of the problem.

(Continued on following page)

(Continued from preceding page)

A point not fully appreciated is that mental retardation, cerebral palsy, and epilepsy are all manifestations of neurologic disease. They are most properly viewed as the major symptoms and signs of diseases of the brain which occur during infancy and childhood (just as vomiting of blood or coughing are symptoms of diseases of stomach and lungs, respectively). Identical neurological manifestations such as mental retardation may be due to any one of several diseases—among them, head injury, lack of oxygen or suffocation, infectious diseases, etc. Therefore, if one tries to promote interest in the study of mental retardation, inevitably, he turns to programs of research in pediatric neurology.

The importance of pediatric neurology and the scientific study of brain disease in infancy and childhood and of such conditions as mental retardation has been recognized for some time at Massachusetts General Hospital, both in neurological and pediatric services. However, only in the past 3 to 4 years have measures been taken to establish a sound clinical and research unit.

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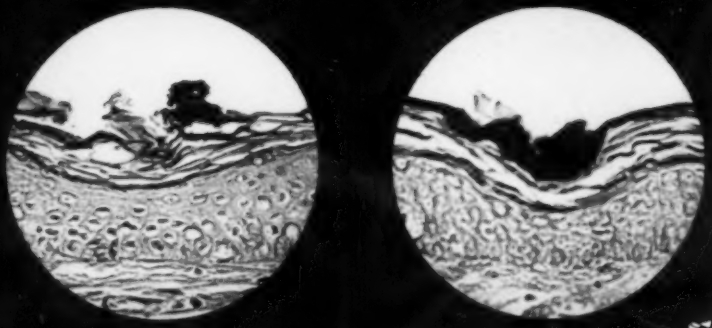

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Treatment of Dystonia Musculorum Deformans Progressiva

WINTHROP M. PHELPS, M.D.*
Maryland

THE PURPOSE of this paper is to delineate this condition as an entity and to report results of treatment.

The interest of the author was stimulated in 1937 by its general similarity to the athetoid type of cerebral palsy.

The failure of any effective treatment has been noteworthy. The twisting or torsion-like involuntary motions have given the condition its alternative name of "torsion spasm". The history of insidious onset at about the age of six years, in a previously normal child, with no history of illness or any other associated symptoms, clearly differentiates it from athetosis. It is most frequently confused with Wilson's disease or hepato-lenticular degeneration. As will be seen, it is extremely important to differentiate the two conditions since they are not related in any way.

Wilson's disease, is, briefly, a degenerative disease involving the lenticular nucleus and associated with cirrhosis of the liver and the Kayser-Fleischer corneal ring, which is a brownish or yellowish green pigment in Discemet's membrane on the posterior surface of the outer margin of the cornea. The condition has been supposed to be due to a disturbance of copper metabolism. It begins also insidiously at the age of about six years also in a previously normal child, usually starting in the upper extremities, with jerky involuntary motions, progressing to generalized involuntary motions including emotional lability, fixed smiling, convulsive laughter and jerky speech. Post-mortem findings are, as the name would indicate, lenticular degeneration and cirrhosis of the liver.

True dystonia musculorum deformans progressiva, on the other hand, begins as a twisting of one ankle. Attempts to strap or brace this ankle are not tolerated and seem only to increase the violence of the involuntary motions. Characteristically, the patient is able to walk until the process extends usually next to the opposite hip.

* Founder, Children's Rehabilitation Institute, Inc., for Cerebral Palsy, Baltimore, Maryland

At this stage, further walking becomes impossible because of the strong and unpredictable flexion motions of the hip. The patient is hardly able to get around even with crutches because he cannot trust either leg. Gradually the other joints of the legs become involved and finally torsion and hyper-extension of the trunk results in the patient becoming bedridden because of the difficulties even in sitting. Often they will lie for hours holding one foot, apparently in an attempt to control the unwanted motions. In the most advanced cases, the motions have become so severe that the patient cannot remain on a bed, and in two of these seen, lying in an empty bathtub, padded with blankets was the only place they felt safe. One patient spent a year in such a bathtub. These patients usually died in early adolescence, apparently from exhaustion, since no consistent findings were determined post-mortem.

It is noteworthy, that, unlike Wilson's disease, the arms are almost never involved, except by the twisting of the trunk and there is never found any involvement of the cranial nerves. Speech, intelligence and emotional stability are normal. Also, there are no liver changes or corneal rings, and no sensory changes and the EEGs are normal.

There is very great confusion in the literature regarding this condition. The term "dystonia" which is a general term, of course, is so loosely used that the reported post-mortem findings extend from extreme generalized brain degeneration to completely negative findings. It would seem that if brain degeneration has taken place that clinically there would be some evidences of cranial nerve involvement, emotional lability or other changes as seen in Wilson's disease, post-encephalitic states or cerebral palsy.

Hassin,[1] in his paper, had come to the conclusion that dystonia musculorum deformans progressiva was not morphological but a physio-chemical disturbance—a purely muscular phenomenon. Alpers,[2] describes the onset, beginning in one foot, and states that the condition is often confused with hysteria. Wechsler,[3] notes that it spares the face and speech muscles. Brain,[4] in London, notes that torsion spasm was first described by Schwalbe in 1908 and that it was originally thought to be limited to Russian Jews. However, at least one-half of my patients have no traceable Jewish blood.

Many other contributors to the literature have used the term "dystonia" in a broad sense, describing it as seen after encephalitis and mentioning cirrhosis of the liver and brain degeneration as a

part of the picture, thus including in the term, post-encephalitic disorders and Wilson's disease again.

On the basis that this condition is a physio-chemical change and muscular in origin, Hassin,[1] in 1939, began treatment with quinine rather empirically because of its effectiveness in Thomsen's disease (myotonia) which is likewise thought to be physio-chemical in nature. He described an eight year old Jewish girl in whom the process had started in the foot. She was greatly improved and the motions controlled. The recent paper by Pachomov,[6] on studies of Dystrophia myotonica, demonstrated definite improvement in some of these by the use of quinine. Hassin,[1] also used quinine in cases of spasmodic torticollis with good results.

In 1937 the author began to use a combination of vitamins B6 and E in dystonia musculorum deformans progressiva. It was noted that these vitamins were completely ineffective in the dystrophies but believed they merited a trial in dystonia. In the follow-up, it became evident that the progress of the condition was halted at the stage at which medication was started. There was, however, no reversal of the condition. Following Hassin's work, quinine was added to the vitamin medication, and in some of these cases, more or less reversal of the condition took place. In others there was little change, but continuance of the vitamin therapy stopped progression.

Very careful muscle-joint examinations are necessary to determine whether the condition has progressed or not. Physiologically the distorted positions of the patient may become more pronounced because the constant motions of one set of muscles, the extensors of the back, for example, will so over-strengthen these muscles that their antagonists, the flexors, become weakened by over-stretching. This increasing deformity is quite different from extension of the condition to other joints. By the judicious use of physiotherapy to reverse the distorted positions and training of the over-stretched antagonists in their shortened position, much of this deformity can be prevented. The methods used by the Bobaths,[5] (reversal of pathological reflexes) is especially adaptable to the physiotherapeutic phase of this condition, although these involuntary motions are not actually "pathological reflexes", since the condition is not of central nervous system origin. Obviously physiotherapy will not cure the condition but help to prevent the contractures which develop from the muscle imbalance.

In considering the possible etiology of the condition, familial disease can be excluded in the author's series. In none of the twelve cases followed for a minimum of ten years, was there even a remotely similar condition present in either side of the family as far back as could be traced. In more recent cases, the same is true, but in one instance there were two children affected in one family. These were very carefully studied to rule out any other type of progressive disease.

With regard to nationality, seven of the fourteen cases were Jewish, while seven were definitely not. One case was in a negro. Nine cases were male and five female.

Developmental or congenital etiology would seem unlikely, since all of these were completely normal up to the age of 4-6 years.

Infectious disease etiology is not likely, since there was never any history of any sort of illness preceding the onset. This is equally true of trauma. No abnormalities of general metabolism or endocrine function can be found.

Toxic disease is unlikely because on careful study there was no history of unusual eating habits.

The most probable etiology would, therefore, be a deficiency disease of some sort because of the response to vitamins B6 and E. B6 or pyridoxin hydrochloride deficiency produces convulsions experimentally in animals. Vitamin E deficiency results in considerable muscular weakness and is used in connection with threatened abortion, both in animals and humans. The combination of B6 and E seems to have a tendency to increase muscle tone in atonic states but the combination shows little or no effect in amyotonia or in dystrophy. It has been suggested that there is some synergistic action when the two are given together but what relation this has to the control of spread of dystonia musculorum deformans progressiva is completely unknown.

In the author's series of cases observed for long periods of time, no advance or spread of the condition has been noted on careful re-evaluation as described.

The fourteen cases seen in the period from 1936 to 1953, which have been followed to the present, all showed no advance in the condition after starting on B6 (pyridoxin hydrochloride, 25 mg. daily) and Vitamin E (alpha tocophorex, 50 mg. daily) to the present time.

PATIENT	FIRST SEEN	ONSET	RACE	ALL STALLED BY BG & E	QUININE TO TOLERANCE (6-30 gr. daily)
1. J. Mh. ♂	1936	1930	J	Bathtub	Some reversal; walks with crutches.
2. V. DW. ♂	1936	1932	NJ	Ankle, hip, trunk	Almost complete reversal; independent.
3. A. K. ♀	1937	1936	NJ	Legs and trunk	No reversal. Helped with Artane.
4. M. J. ♀	1938	1936	NJ	Legs	No reversal. Helped with Artane.
5. C. K. ♀	1940	1940	NJ	Ankle	No reversal. Helped with Artane.
6. M. J. ♂	1942	1945	NJ	Spastic hemiplegia, legs and trunk	Intolerance to Quinine.
7. R. P. ♂	1943	1943	NJ	Ankle and hip	Definite 50% reversal; independent.
8. J. Mn. ♀	1945	1942	J	Bathtub	No reversal. Helped with Artane.
9. M. M. ♂	1945	1943	J	Legs and trunk	Definite 50% reversal. 30 grains.
10. T. R. ♂	1950	1947	NJ	Ankle, trunk and neck	50% reversal.
11. M. ♂	1950	1948	N	Legs and trunk	No reversal. Helped with Artane.
12. S. M. ♂	1952	1951	J	Legs and trunk	No reversal. Helpless after chemopallidectomy.
13. R. S. ♂	1952	1951	J	Legs and trunk	No reversal. Helped with Artane.
14. J. G. ♀	1953	1951	J	Legs and trunk	Slight reversal with Quinine

The degree of the condition when first seen varied from early involvement of the ankle only to complete involvement of legs and trunk, and two cases were extreme, necessitating bathtub confinement. Both of these have improved to a considerable extent, leading active lives. Both of these now walk with crutches.

The time first seen after onset varied from six years after onset in one of the bathtub cases, to a few weeks after onset in the case in which the ankle only was involved.

Reversal of the condition with quinine in doses beginning with 6 grains daily and working up to tolerance, (in two cases up to 30 grains daily), was seen almost completely in one case, with definite improvement in five others. In one case there was a definite intolerance to quinine. Bleeding and clotting time was checked at six-months-to-yearly intervals and vitamin K administered if necessary. This was only necessary in one case and quinine was discontinued. In the other seven cases, there was no change in the condition, even after prolonged use of quinine.

These seven cases have had some decrease in the condition by the use of Artane (tri hexy phenidil) but the results have not been spectacular.

Age at onset in all cases was between 6 and 8 years, and all began in one ankle. All EEGs which were taken were normal and there were no neurological changes in any except the one case in which a spastic hemiplegia was present previous to onset of the dystonia. It was felt that this was purely coincidental. The patient had been seen by the author previous to the onset of dystonia.

SUMMARY

Dystonia musculorum deformans progressiva is

(1) an entity—probably a physio-chemical disturbance, not of central nervous system origin.

(2) This condition must be carefully distinguished from other conditions producing involuntary motion, especially Wilson's disease, post-encephalitic conditions and athetoid cerebral palsy.

(3) The condition in 14 cases followed from 5-20 years did not progress after continuous medication with large doses of vitamins B6 and E.

(4) Reversal of the condition took place almost completely in one case and partially in five others by the use of quinine.

(5) In those not reversed by quinine, Artane was helpful in reducing the force of the motions when combined with the continuous administration of B6 and E.

CONCLUSIONS

On the basis of previous reports and clinical results, dystonia musculorum deformans progressiva is believed to be a physio-chemical change, not of central nervous system origin.

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How Occupational Therapy May Aid the Pediatrician in the Development Appraisal of the Child

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GROWTH of the child is the best estimation of its development and is self conditioning. Past growth modifies present growth and both project themselves into the future. It is for this reason that psychological growth of the child becomes a series of patterned events that are outwardly manifested by behavior. Thus the nervous system is a vital part of the mechanism that makes these events possible. The developmental approach therefore holds for cultural guidance controls; but it is based on a good understanding of growth which is mainly a series of events governed by laws and forces. It is in the observation and interpretation of this sequence of events that the occupational therapist can be of considerable aid in the development of this appraisal.

A baby follows a dangling object with his eyes. Formed connections have been made between his nerve fibers and muscle fibers. Later he will attempt to grasp the object with both hands, and at a later date reach with one hand only. Later the still older baby may poke a small object with his extended index finger. These are well defined responses of the neuromotor system to a specific situation. It is a process which progresses with an orderly sequence. Inasmuch as it is quite necessary for the occupational therapist to be completely aware of the child's capabilities, conversely an accurate knowledge of these are of the utmost importance in any appraisal of the total developmental concept.

Perhaps the child has been referred to the occupational therapist for the development of physical activity of the lower extremities. His age gives her a beginning frame of reference when she first observes the child. However, it is necessary for her to know if the

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desired activity should be one involving crawling or walking. Will the railing of a playpen allow maximum activity, or will a pull toy, and space to ramble in provide better treatment? If the therapist is aware of the sequence of development for a normal child, she can intelligently observe the child as well as give him opportunities to show what he is ready to do. In the same manner other aspects of motor development can be more easily understandable when it is learned what to expect from the normal child and to observe what that particular child accomplishes. If he puts a cube in a cup, and takes it out again without releasing it, then we would not expect him to be interested in stack toys. Inasmuch as he has not learned to release an object at will, he has not learned that one thing can fit into another. Developmental evaluation then, is a guide for more effective treatment.

The child's reaction to frustrating situations can be evaluated. How does he react when his tower of cubes tumbles over? Is he distressed when one falls on the floor, or does he get down and pick it up? Does he say he can't do it before he even tries, or does he try to solve the problem the best he knows how? The consideration of his emotional capacities in relation to his cultural background, will begin to give him experience that can build his self-confidence. This is an important factor in effective treatment.

Just as one aspect of the child is intricately involved in his overall behavior, so the child as a whole is seen only in the total of responses to the developmental appraisal. The physical needs of the child can best be appraised if we also weigh all of the other aspects of development. When we consider social behavior, we must include all of the child's personal reactions to the social culture in which he lives. This should include his home environment even more than the hospital situation which after all is only a fleeting though impressive moment in his life. Social behavior can be appraised by his socialization. First, there is the solitary play of the infant while in the immediate vicinity of his mother, followed by the parallel play of the 2-year-old who is absorbed in his own activities. The 3-year-old indulges in associative play as he begins to realize that the world "is not all for me". Finally at the 4 year age level, we find the beginning of cooperative play, which becomes more complex as the child becomes older. The ability to do what is expected of him in the presence of adults, involves neuro-motor maturation as well as a certain amount of gratification received in return for his performance. We could not expect the child to wash the back of his

hands clean after finger painting when he has not as yet developed a controlled wrist motion as illustrated by the stiff way in which he throws a ball or turns a door knob. Here again the developmental evaluation gives us guidance for more effective therapy.

Language is another aspect of growth and development that colours all other aspects. Mother gives us clues here. The informal interview with the mother is a necessary and informative part of the developmental appraisal. The questions should be so phrased that their meaning is clear and correct without being suggested, and should be phrased so that the mother is not too embarrassed by her inability to reply in the affirmative. She can tell us what the child calls himself, does he wave bye-bye, does he have any words for his toys or food, is he putting two words together, or other pertinent information. With direct observation we can ourselves observe the response to his name, see him pat-a-cake, listen to his jargon or hear the length of his sentences as he tells the story from the picture book. We learn his ability to understand what is meant by the prepositions "under, on top of, beside, or in back of" and his comprehension of the abstract. The sequence is a logical one and in sufficient detail to give us the trend of behavioral development.

There is one more area which we should consider in demonstrating the value of the development appraisal by the occupational therapist to the pediatrician. Drawings give us further insight into the growth status of the child. Although we are unable to interpret the psychological import of his drawings, we can learn valuable information in terms of neuro-muscular maturation. A further inclusion would be graphic representation, general development in observation, and his learning ability and individuality. In the preschool period there is some evidence that creative drawing ability may be unrelated or even inversely so to eye-hand coordination skills since imagination is essential for all creative activity. Perhaps the inaccuracies of the child with poor eye-hand coordination might stimulate the imagination of design and challenge him to further interest and effort in art. The year old child may bring the crayon to the paper but does not always leave his mark. He may hit rather than mark the page. By 1½ years we may see less banging and more scribbling which is not confined to the page.

The child at the 2 year age level is able to control the crayon within the confines of the paper, but his marks may be small or large, round or straight and sometimes in all directions. The 3 year

old will imitate the vertical and horizontal strokes. He still holds the crayon awkwardly but the fingers are beginning to curl under for better support of the crayon. This means a representative drawing, but one that still must be titled to be interpreted. He can match the color forms long before he can draw them. This requires neuromotor maturation of the eyes, not the hands.

The drawing of a 4 year old will begin to take a definite form. It still needs to be titled and even interpreted, but the circles in the potato shaped head are the features of a man. Now it is clear that the child is organizing his graphic representation to conform to his idea of a person. This involves concentration and effort, and may even be upside down in orientation, but there will be increased detail of body, ears, and even two dimensional legs. The 6 year old child will finally show a mature grasp. The dimensions of the figure will become more accurate giving the impression that the man grows up with the child. More detail is illustrated by the clothes, fingers, laces, teeth and two dimensional nose. Such drawings will not necessarily typify those of all children at the specific ages, but it does show the general sequence of maturation and graphic representations.

In the aspects of the developmental appraisal discussed, namely the motor area, adaptive area, and language and personal social areas, growth sequence is not yet complete. Human behavior can be evaluated only in the sum total of its component parts, but with only a few of those parts we do not find an equal appraisal of growth and development. The portion of time, then, that the therapist takes to present the standardized play materials to the child has usefulness of its own. It is a time when the child is stimulated to do his best in return for the complete attention of the therapist. He feels a sense of security by the acceptance of his efforts. He has little to distract him and the change in activity will be adjusted to his attentive capacities. The therapist frequently finds that from that half hour or so she knows this child as an individual with certain capacities, abilities, and personality traits; and she finds that she has perhaps gained some rapport with him. From the child and the mother she discerns habit patterns that can be used or emphasized; habits of play, habits of feeding, dressing and toilet. Not only does the developmental appraisal serve as a diagnostic aid, but has treatment value as well; for if the therapist is alert in her observation and at the same time attends to the needs of the child, both the child and the therapist will gain by the experience.

If the child has a physical disability which prevents or distorts a part of his motor abilities, it will be essential to work with him at two or more levels of performance. Perhaps the child is at the level of a 2 year old in ambulation, and at a 4 year old in manipulation, while his chronological age is actually 6 years. This same child of 6 years may be at the level of a 2 year old in all areas. His developmental appraisal would give a baseline for setting up adequate therapy. The goals would be apparent. A child may be referred to therapy for standing table experience. From the appraisal the therapist sees that the child has head control but does not as yet have good trunk control. The abilities of this child will give her a good idea of where to start. Of course the appraisal does not stop there for therapy requires a continuous evaluation with adjustments following more mature performance.

Assuming then that we know where the child is in the course of growth and development, we have an excellent opportunity to incorporate this information into treatment procedures. A child age 2 years 7 months may be referred to therapy by the pediatrician, for walking experience. We know that the child has good balance in sitting but does not have standing balance or reciprocal motion required for walking. We also know that she is performing at an age level of from 18 months to 2 years. The therapist takes her cue from the child's interest in throwing the ball, using this as the incentive for creeping which allows practice in four point balance and reciprocal motion.

Another child may be referred for activities to increase muscle power and range of motion of the upper extremities. She is 3 years and 4 months old. We learn that she has the capacity and interest of a 4 year old in fitting shapes together, matching and building We also understand that she is beginning to play cooperatively with another child and her favorite toys at the moment are imaginative play materials. We can begin to shape our treatment plans. The therapist may play with her alone for awhile by handing her the various pieces of a stack toy which she puts together and takes apart to hand back to the therapist again. Perhaps a weighted doll is put to bed requiring repeated lifting and setting down. The therapist may bring out the clay to be used as play food for the toy dishes but is actually helping to weight the dish that the child wants to set on the toy stove. The stove and bed may be placed at a height which requires maximum range of motion. Many of the play situations are adapted in this manner for gaining the objective

of the prescribed therapy in terms of the developmental needs of the child.

Adjustment to the hospital is a nebulous objective often requested of the therapist in the hospital setting. She can do very little until she learns two things. First, what are the symptoms of the child which cause the request for the therapist's attention; and secondly, what are the needs, capabilities and environmental background of this child. The former question is, of course, answered by the referring pediatrician, but the latter question is answered gradually by several means. First, by interview with the parents, and secondly by evaluation of present capacities of the child and by the evaluation of his problems imposed in view of his cultural background and developmental status. Here the developmental appraisal—that is, the time consumed in evaluating the child in controlled situations—has treatment value. The child is thus developing a personal relationship with the therapist and through this, learning a part of what it means to be in the hospital.

The therapist knows how to make each of the appraisal situations a positive experience for the child, since she is concerned with those things which the child is doing and not what it can or can't do. When the appraisal is completed she knows how to set up the child's environment for best treatment results. An individual child is not able to tolerate sharing his toys with another child although mother says he does share with his brother at home. The therapist makes sure that his playthings need not be shared. She limits the amount of give and take required of him by creating opportunities for him to play alone and become acquainted with the therapist, playroom and toys. Later when the child has developed indications of readiness, other children may be added for activities in parallel play, and still later conditions may be introduced to the activity which requires further sharing with others. During this time the therapist lends her support or stays in the background according to the children's needs. The therapist finds that the appraisal has treatment value in that she knows what the child does in lieu of what the pediatrician wishes for the prescribed treatment.

However, the entire picture of the child must be considered, or an incomplete evaluation will be obtained. On the first day of admission the admitting pediatrician learned that a 2 year old child could count to 10. Each person that met the child that day praised him for the accomplishment, and consequently began to think of

him as a precocious child. In the days following everyone was baffled by his childish behavior. He cried whenever he was not held, would not play with the other children, and even refused to go into the playroom. He was referred to the occupational therapist for help in adjustment to the hospital. The treatment is obvious but it does point out the danger of a hurried and incomplete evaluation.

The information derived from a developmental appraisal gives the therapist points of reference in planning and carrying out a treatment program in activities of daily living. A 3 year old blind child may not be able to tell you the names of pictures in a picture book, or run well without falling in a strange area, but from a complete evaluation we find that within limitations of the disability he is performing at about a 2 year age level. We know then, that the therapist's efforts will not be directed in teaching the child to put on his shoes or button his clothes, but will be directed in pulling on simple garments. She will praise him for a good job even if the child does get his sweater on backwards, because she knows that it will be some time before he could be expected to distinguish the front from the back.

The developmental appraisal may be of great value in serving as a base line for the judgment of later development. A 5 year old child was admitted to the hospital with untreated hypothyroidism. She was about the size of a year old baby and had the usual dry skin, coarse dry hair, enlarged protruding tongue, and a lethargic apathetic nature. She drank from a bottle and slept most of the day. She did not walk or talk. She was referred to the occupational therapist for developmental guidance following initial therapy. The pediatrician requested that specific attention be given in providing stimulating activities to correspond with the rapid growth and development expected from medication. She soon began to show changes by reaching for her bottle, moving around in bed and staying awake for longer periods of time. In a week she was attempting to crawl on the floor and preferred to be in the playpen during waking hours.

A developmental appraisal was completed after the maximum dosage of thyroid was regulated. In the motor area her age level was about 15 months. Her interest in books was concerned with manual activity, turning pages, turning the book over, opening it backward, and so forth. She was particularly engrossed in small

objects such as the pellet and string. She would pick them up with an inferior pincer grasp. The cubes held less interest but she would line them up or grasp them in several experimental ways. She loved to have someone hold both hands while she would attempt to walk, but otherwise moved about on both hands and feet, discarding the usual method of crawling.

In adaptive behavior she performed at about a 15 month age level, imitating drawings which resulted in circular and vertical strokes, while holding her crayon in her fist. Her concept of fitting three dimensional forms in the formboard was not clear but she did take out and put in the round block. She liked to put the blocks in the cup and dump them out again. She discarded her bottle and drank from a cup alone and ate successfully with a spoon.

The appraisal served two purposes. It gave the staff a baseline for later comparison, and it gave the therapist guides for better treatment. This treatment consisted of a wide variety of activities and toys. Further opportunities for growth and development were allowed in all areas with less emphasis on walking which had been the main objective of the entire staff for this child.

She was readmitted for evaluation when she was 6½ years old. She looked about 3 years of age, and had developed a happy, good natured personality. She was not easily provoked to tears and was affectionate with anyone who gave her attention. She tended to go out of bounds at times in a provocative way. Her interest in the appraisal equipment was strong and she followed directions using independent judgment when she objected to the requests. She walked alone and was usually seen running or climbing. She managed to build an 8 cube tower but lacked coordination to build it higher. The formboard was completed after several errors. She preferred to play in parallel activities with the other children, could pull on her own dress and shoes, was toilet trained and verbalized her needs fairly consistently.

However, if we examine her developmental quotient we find that in her first appraisal she had developed to 25% of the norm for a 5 year old child, and on the second evaluation to 30% of the norm for a 6½ year old child. This slight gain is negligible when we consider that the child was in an environment more conductive to normal development by being at home for a year and a half. The role of the occupational therapist here is perhaps a negative one, in that the lack of developmental acceleration is made more evident.

However, it is valuable in emphasizing the guiding limits to be set; so that acceptable patterns would not be forced on the child which would tax her limit of capacity.

CONCLUSION

Growth and development does not run a smooth course but has its ups and downs. It is sometimes difficult to see progress in a child with whom you are working closely. Little incidents in the child's life cause back slides or temporary regressions to former more comfortable behavior. At other times he surpasses himself in attaining new heights of development. The natural trend is toward a greater maturity. In the field of pediatrics certain methods have been developed by occupational therapy for evaluating the capabilities or potentialities of children. Some of them are check lists, some are tests and some are guide outlines. All of them help the therapist to guide treatment and delineate objectives. They can serve as a base line for later comparison and may be outlined by the developmental appraisal, thus becoming of great aid to the Pediatrician.

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Dysostosis Multiplex

REVIEW OF LITERATURE AND REPORT OF TWO CASES WITH UNUSUAL MANIFESTATIONS

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DYSOSTOSIS MULTIPLEX is a rare disease of which until 1950 only about 150 cases were reported.[1] It results from a metabolic disturbance and its manifestations show in the skeleton, as well as in the soft tissues.

The purpose of this article is to review briefly the condition and to present two cases with unusual manifestations.

Historical Review: The syndrome was first described by Hunter (1917)[2] as "A Rare Disease". Two years later it was fully annotated as a separate clinical entity by Gertrude Hurler (1919).[3] It was named "Dysostosis Multiplex"by Binswanger and Ullrich (1933),[4] and because of the characteristically inhuman facies, Illis, Sheldon and Capon (1936)[5] suggested the name "Gargoylism". In 1934, Tuthil[6] described the storage of a lipoid-like material in the brain cells and hence the name "Lipochondro Dystrophy" was given by Washington (1948)[7] to the condition.

Etiology and Pathology: The disease has no race limitations or preferential sex. It is genetically determined. Its frequent occurrence in siblings and the number of cases in which consanguinity of parents has occurred, point to a recessive inheritance by a single gene.

As a result of an inborn error of metabolism, there is over-production of an abnormal material which gets stored in the cells of many organs. This material was first thought to be a lipoid. Later, Strauss' studies[8] suggested that it might be a non-lipoid of a high molecular weight such as glycogen and recently Lindsay *et al*[9] presented certain histo-pathological data which suggest that it is glycogen combined with a protein. More recently, however, the material has been identified as an acid-mucopolysaccharide.[10]

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The material commonly accumulates in the liver and spleen producing hepatosplenomegaly, in the lymph nodes, the brain, the anterior lobe of the pituitary, the cornea, the heart, the blood vessels and the skeleton including the periosteum.

The stored material appears as large vacuoles in the cells of these tissues and in this disorder it is the parenchymal cells and not the cells of the R.E.S. which are the main seat of affection and in this respect Gargoylism differs from Lipoidosis.[1]

In the cornea, it can be seen by the slit-lamp that the material is deposited in the deeper layers as small, uniformly distributed refractile particles.[11,12] The epiphyses show slow growth and irregularity of the zone of proliferative cartilege, giving an explanation for the lack of growth and for the irregularities at the end of the diaphysis and for the abnormal formation of the articular surfaces. The cartilages of the vertebral bodies also grow in an abnormal way and flattening and malformation of them occurs, especially in the regions where the mechanical pressure is greatest, such as the junction of the thoracic and lumbar parts, which is the usual site for kyphosis. Lesions in the skull are difficult to explain. However, abnormal growth of the parts formed from cartilage certainly play a role.

Clinical Features: Although the condition is congenital, the child usually appears normal at birth and during the first 3 to 4 months of life. The gargoyl has a peculiar facies characterized by a big skull, prominent supra-orbital ridges, depressed nasal bridge, broad nose, constant nasal discharge, narrow palpebral fissures, cloudiness of the corneas and thick tongue and lips. The neck is short and thick, the spine is kyphosed and the limbs are short. The joints show limitation of movements particularly of extension. Usually the hands are claw-shaped while the feet are everted.

The fully developed case usually shows osseous and soft tissue manifestations.

I—Osseous manifestations include:

i—Deformities of the skull.

ii—Deformities of the vertebrae leading to kyphosis and this is usually the earliest sign to appear.

iii—Deformities of the extremities.

II—Soft tissue manifestations include:

i—Ocular manifestations of which the most constant and

pathognomonic is bilateral cloudiness of the cornea which cannot usually be detected before the age of 1-2 years. Less commonly, there may be elevation of tension,[13] buphthalmos[14] and megalocornea.[15,16]

ii—Central nervous system manifestations; namely mental retardation and occasionally hearing defects. The latter usually begins between 6-12 months of age.

iii—Enlargement of the liver and spleen and this is usually marked, causing protuberance of abdomen and umbilical hernia.

iv—Skin changes.[17] These, when present, usually appear during the first year of life and they include thickening of the skin, lardaceous eczematoid dermatitis of the face and hirsutism. The external sex organs may appear normal but sexual maturation does not occur.

Cases with incomplete and less striking manifestations "Fromes Frustes"[1] are not rare. In the reported cases clouding of the cornea was absent in 30%, mental defects in 10% and enlargement of the liver and spleen in 20%.

Laboratory Data: In about half the cases, there are abnormal granules in the W.B.Cs. (Reilly bodies). They take a dark lilac color when stained by the Geimsa-Wright technique (Reilly 1941).[18] The urine may be positive for mucopolysaccharides. Other laboratory studies including liver function tests and lipid content of the blood,[20] usually show no characteristic changes.

Radiological Findings: The skull is usually scaphocephalic, large and massive and the sella turcica is usually elongated without increase in depth. The spinal column shows kyphosis due to deformity of one or more vetebrae, which show a peculiar hook-like process in place of the anterior half of the body. The long bones are stouter and shorter than normal and their epiphyses are expanded and may be set at an angle giving rise to enlargement and deformity of the joints. The metacarpals and metatarsals are broad and short, the basal phalanges are usually cylindrical while the distal ones are often conically pointed. The bones of the pelvis are usually small and infantile and coxa-valga may be present. The glenoid and acetabular fossae may be poorly developed and the heads of the humeri and femora may be flattened.

During the first year however, X-Ray pictures may not reveal anything abnormal.

Treatment and Prognosis: The prognosis is unfavorable since the great majority of these cases die before the age of 20 years. Death is usually from some cardiac or pulmonary disease, generally speaking the condition is uninfluenced by treatment. However, the orthopedic surgeon may help by correcting the kyphosis while the ophthalmologist may remove a serious symptom by corneal transplantation.

CASE REPORTS

The two cases to be reported are brothers (Fig. 1). They are the second and fifth children of healthy, middle aged parents who are related. Their other two brothers and sister are normal and no similar condition is known in either parent's family.

Fig. 1

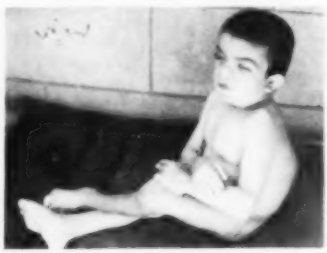

Fig. 2

CASE NO. 1

This is the elder brother. He is 10 years old. He was born at full term after a normal labor. He looked normal at birth and was thought to be so until the age of 7 months when eversion deformity of the feet was noticed. At one year age, deformity of the hands and fingers started to show and at 2 years, kyphosis became apparent. Since 3 years the facial appearance began to change and since 1.5 years hearing is diminishing. He has a normal sphincteric control. However, his mother is aware that his mentality is below that of his younger brother aged 8 years.

Examination showed a dwarf with a large head and reduced body weight (104 cm. height, 54 cm. skull circumference and 23.5 kgm. body weight as compared to normal of 130 cm., 51 cm. and 30 kgm. respectively). The patient was apparently mentally defective but was able to understand some simple requests. He had a peculiar grotesque facies (Fig. 1) with a big skull, thickened and ptosed upper lids, heavy cheeks, depressed nasal bridge with widened nares, much thickened and everted lips, big tongue and widely spaced and irregularly placed teeth. Nasal obstruction

was marked, speech was heavy and hearing seemed to be impaired. There was no cloudiness of the corneas and the following is the report of the ophthalmologist on the condition of the eyes;

i—There is congenital glaucoma on both sides (Tension on Rt. side 27 and on Lt. 32).

ii—Corneal diameter 13.75 mm. on Rt. Side and 14 on Lt. (normal is 10-11).

iii—Congenital cataract on both sides.

The heart and lungs were clinically free but the ECG showed auricular extra systoles. The liver was only one finger below the

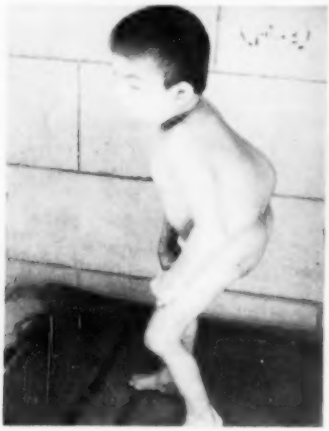

Fig. 3

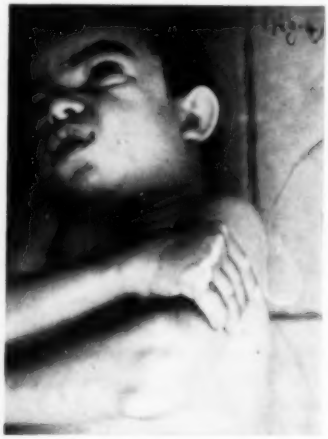

Fig. 4

costal margin while the spleen could not be felt. The abdomen was not protuberant but the abdominal wall was very tight and tough. The patient had a severe lumbar kyphosis and his hips and knees were kept partially flexed (Fig. 2, 3) and this made him unable to stand or walk unassisted. In the limbs the outstanding features were enlargement of the big joints, especially the elbows and knees (Fig. 2, 3, 4), with limitation of all movements but principally extension. The hands were claw-shaped and on the left side the ring finger was severely incurved (Fig. 2, 5).

The musculature of the extremities was poorly developed and the quadriceps muscles were much tightened and toughened by the infiltration.

The skin changes in this case were very marked and peculiar, and we are therefore going to report them in some detail:

1. In the face: The skin of the forehead was sclerosed and showed papular red eruptions. The skin could not be pinched. The subcutaneous fat was diminished. The cheeks were much thickened and infiltrated and showed a marked hair growth. The skin of the chin was much thickened and sclerosed by the infiltration and showed some reddish yellowish itchy papules. The upper lip was much infiltrated and the gums were thickened.

2. In the neck: The skin was much thickened and infiltrated and showed discrete papules.

3. Over the trunk: The skin was much less affected. The subcutaneous fat of the breasts appeared normal on the right side and showed nodular infiltration on the left. The skin of the abdomen, especially on the left side was very tight and tough. On the other hand, the skin of the back was nearly normal except for excessive lanugo hair over the shoulders.

4. In the limbs:

a) In the upper limbs the skin was very tight and marked lichenification was seen near the elbows on the extensor surfaces. Small subcutaneous nodules could be seen and felt (Fig. 4) along the subcutaneous borders of the ulna and radius on both sides. These were painless hard pellets in the size of mellet seeds. They seemed to be fixed to the underlying bone.

There was also hirsutism and that was especially marked over the extensor surfaces especially near the elbow region.

b) In the lower limbs, the skin was tight especially on the extensor surfaces. Nodules similar to those described above were noticed along the shin of the tibia. Hirsutism was also marked especially below the knees where blotchy brown melanotic patches could be seen.

c) Over the palms and soles, the skin looked normal, except for collosities formed by pressure over the prominent deformed areas.

Laboratory Investigations: Blood picture revealed nothing abnormal. W.R. was negative. Blood lipid studies and glucose tolerance test gave normal results. Blood calcium, phosphorus and phosphatase were all normal. Urine showed no abnormality. Biopsies were taken from: 1) the liver, 2) the skin of the chin, 3) an enlarged hard cervical lymph gland and 4) one of the nodules

over the subcutaneous border of the left ulna. The histopathological report was as follows:

1) The liver showed no abnormality.

2) In the biopsy taken from the skin of the chin, the epidermis was stretched and showed absence of rete pegs. It also showed hyperkeratosis. There were groups of large vacuolated cells in the superficial and deep layers of the dermis which contained dense collagen fibres. The subcutaneous tissue also showed groups of vacuolated cells separating small groups of muscle bundles and strands of fibrous tissue.

3) The lymph gland biopsy showed a thick fibrous capsule and evidence of dense fibrosis which in some areas appeared homogenous and cartilage-like.

4) The subcutaneous nodule biopsy showed groups of vacuolated cells separating dense fibrous tissue.

Fig. 5

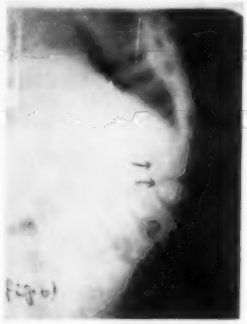

Fig. 6

X-Ray pictures showed the following positive findings:

1—The skull was big and massive and an encephalogram showed a uniform dilatation of the ventricles of a moderate degree.

2—Kyphosis of the spinal column with hook-like bodies of the first and second lumbar vertebrae (Fig. 6).

3—The pelvis showed wide symphysis, flattened acetabular fossae especially on the right side where posterior dislocation of the hip joint was noticed (Fig. 7).

4—The long bones were stout and short and their ends were widened and flared giving rise to big and deformed joints (Fig. 8).

5—The metacarpals and metatarsals were irregularly widened, the proximal phalanges were broad while the distal ones were conically pointed (Fig. 5, 9).

Treatment: The ophthalmologist is intending to perform an operation on him for the glaucoma, followed by another for the congenital cataract.

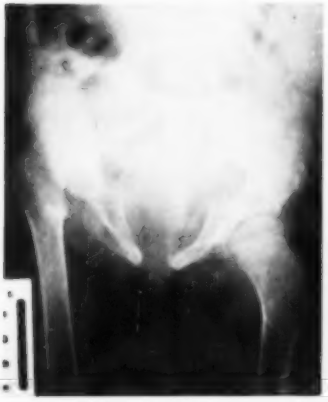

Fig. 7

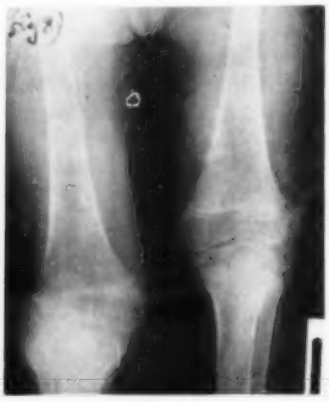

Fig. 8

CASE NO. 2

This is the youngest brother of case No. 1. He is 10 months old and was born at full term after a normal labor. Since birth he had talipus of the right foot but otherwise was normal. Forty days after birth, however, the mother noticed that he was developing exophthalmos with progressive enlargement of the eyeballs and diminution of vision. When 6 months old, kyphosis started to appear. Two months ago, the patient was operated upon for the eye condition with some visual improvement.

On examination the child was 65 cm. height, 6.75 kgm. weight, and 45 cm. skull circumference (compared to the normals for his age, 65 cm. height, 90 kgm. weight and 43.3 cm. circumference). He showed a marked lumbar kyphosis. Mentally he looked normal for his age and hearing was apparently not affected. He showed the peculiar grotesque facies (Fig. 1) with large head, prominent supraorbital ridges, saddle-shaped nose and big anterior nares. He had severe exophthalmos with very big eyeballs but the corneas showed no clouding. The mouth opening was wide and the ears were remarkably big and low seated (Fig. 1). Besides he had the ordinary signs of rickets. The heart and lungs were clinically

free and the liver and spleen were only one finger below the costal margin. The abdomen was not enlarged. The skin manifestations were altogether lacking in this case. The limbs showed no deformities and their joints looked normal and had normal range of movements. However, the hands were somewhat broader than normal and the fingers were broad and short. The following is the report of the ophthalmologist on the condition of the eyes:

i—Bilateral Buphthalmos (congenital glaucoma).

ii—Bilateral Irideucleisis (Iris inclusion operation).

iii—Tension is now controlled. No visual improvement is expected because the case had been a very advanced one (criterion is corneal diameter which is 18 mm. on either side, the normal in the child is 10-11 mm. and in adult is 12 mm.)

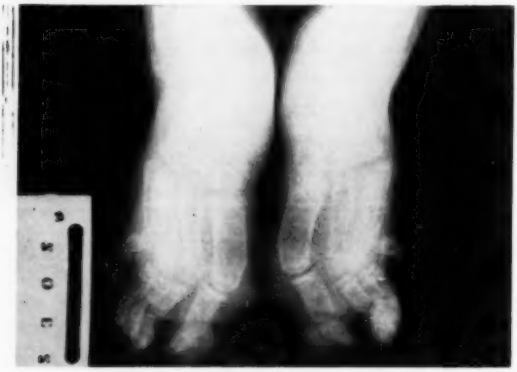

Fig. 9

Laboratory Investigations: As in the previous case, the blood picture, blood lipids and glucose tolerance test gave normal results. However, due to rickets blood phosphatase was high (25 B.U.) and blood phosphorus was low (3.5 mg. %) while calcium was normal. W.R. was negative. Liver biopsy showed no abnormality.

X-Ray picture: The only significant finding was in the spine which showed the characteristic peculiar deformity, described above, in the second and third lumbar vertebræ.

SUMMARY AND COMMENT

A review of the condition of gargoylism is given and two new cases with unusual features are presented. In these cases the following points are noticed:

1. Hepatosplenomegaly is not a marked feature in either.
2. Such widespread and variable skin manifestations as seen in case No. 1 is not common.
3. The subcutaneous nodules described and biopsied in the first case are, to the author's knowledge, not previously reported.
4. The association of congenital cataract (first case), with other eye manifestations in gargoylism is, to the author's knowledge also, not recorded.
5. Absence of cloudiness of the cornea in presence of other rare eye manifestations as congenital glaucoma, buphthalmos and megalo-corneas is rather unusual.

ACKNOWLEDGEMENT

The author would like to thank Dr. El Araby, M., (M.S.O.), Dr. Attia, O. (Ph.D.) and Dr. Badre, M., (M.D.D.) for the ophthalmic, biopsy and skin reports.

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Carisoprodol in the Treatment of Children With Motor Difficulties Due to Brain Impairment

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PATIENTS with motor difficulties due to brain injury are often grouped under the designation of cerebral palsy. They constitute a major challenge to the therapeutic efforts of the clinician. For one thing, there are at present approximately 500,000 victims of cerebral palsy in the United States and thousands of new cases come to diagnosis each year. For another thing, a very large proportion of the patients seen in practice may be quite accurately categorized children with mental retardation due to brain damage, but whose I.Q. ratings are such as to show them capable of undergoing some training. Since these patients are educable, the physician's specific work of rehabilitation often brings direct and gratifying evidence of progress in their general ability to cope with life socially.

Etiologically, these conditions are variable, the causes ranging from Rh factor or birth trauma to postinfections influenza early in infantile life. The basic point is that the brain is both complex and vulnerable—it is subject to damage from factors such as hemorrhage, clots, softening, cysts, adhesions, scars and angiomatous vessels; depending on the kind of brain lesion, its extent and its location, the damage gives rise to cerebral palsy, mental retardation, epilepsy, aphasias, sensory changes and defects of vision and hearing.

The integrative properties of the brain are such that, when one part or area is damaged and thereby limited in functional ability, other parts or areas (uninjured or less involved in damage) apparently assume a compensating role. In so doing, the "substitute" areas may be poorly adapted to their assumed tasks; this very often produces an over-compensation of function, which may become a greater handicap than the original brain damage.

Cerebral palsy may result from any disease process or injury adversely affecting the brain of a child either with respect to the motor system proper (for example, the pyramidal and extrapyramidal pathways), or to the cerebellum, or to both.

In the spastic type of disorder, there is cortical damage in the area that normally controls planned voluntary movements; cases with rigidity are of similar origin, but the cortical lesions are more widespread.

Lesions involving the basal ganglia—normally controlling automatic and associated movements and certain aspects of posture—give rise to conditions of athetotic and choreiform-athetotic types, sometimes with tremor.

The ataxic form of difficulty reflects a cerebellar lesion in the area that normally controls coordination.

Motor difficulties in cerebral palsy are, in very basic terms, departures from the normal muscular function that is characterized by balanced reactions. Thus, when a normal muscle contracts, its partner-antagonist relaxes; the resultant motion is carried out by these interrelated adjustments in muscle tone, which are governed by reciprocal innervation of the muscles in question (Sherrington's Law).

A spastic muscle, however, is hyperirritable and behaves very differently. It reacts adversely to any stimulus, especially a "stretch" stimulus. For example, a spastic biceps may be "put on the stretch" by causing a quick extension at the elbow from the flexed-arm position. Depending on the degree of spasticity, this stimulus suffices to make the spastic biceps contract and halt the motion, or causes it to permit only a slow, interrupted movement.

In the attempt to correct the motor disorders of cerebral-palsied patients, the author became interested in the possibilities of carisoprodol,* a drug with analgesic and muscle-relaxant properties exerted through effects on the central nervous system. carisoprodol apparently has a selective action that favorably affects the antigravity extensors and other muscle groups of the extremities, but without abolishing natural defense reflexes. The drug has been reported in full detail pharmacologically;[1] in the clinical field of cerebral palsy, it has been used with success both here[2,3] and abroad.[4,5]

MATERIALS AND METHODS

The patients in this clinical investigation, all seen in my private practice, were 72 children with motor difficulties due to cerebral

*Soma supplied by Wallace Laboratories, Cranbury, N. J.

palsy. They ranged in age from 1½ to 16 years, with the average at seven years. There were forty-four males and twenty-eight females in the group. Diagnoses, and number of patients per category, are listed in Table 1.

TABLE 1

Results in 72 Patients—Treatment including carisoprodol

Type of Case	Number of Patients	Results		
		Good	Fair	Poor
Spastic	30	23 (77%)	6 (20%)	1 (3%)
Rigidity	22	11 (50%)	8 (36.5%)	3 (13.5%)
Athetoid	14	3 (21.5%)	8 (57%)	3 (21.5%)
Ataxic with Athetosis	3	1 (34%)	2 (66%)	0
Tics of Face and shoulder, with choreiform-athetotic movements	2	0	2 (100%)	0
Ataxic	1	0	1 (100%)	0

Analysis of results is tabulated horizontally in each diagnostic category.

The period of observation for these patients ran from July, 1959, to September, 1960, averaging out to about seven months of study per child, with office visits at intervals of about one month. Since carisoprodol is available for clinical use in two dosage forms—a 350 mg. tablet and a 250 mg. capsule—I tried at first varying the daily dosage and frequency of administration for the older and the younger children in the group. After a few days, however, it was apparent that the most practical and effective procedure was to give all patients the same regimen of carisoprodol. This study is therefore reported on the basis of a uniform dosage—one 250 mg. capsule of Soma twice daily, for each child in the group.

In addition to this carisoprodol therapy, the patients were all under treatment with other measures customary in the author's practice, such as physiotherapy and muscle education, glutamic acid treatment, glandular medication, etc., as indicated for various symptoms encountered in cerebral-palsied children.

Appraisal of clinical progress was made through the observations of parents, physiotherapists and teachers. These were correlated with the author's findings and appraisal of conditions at the office visits.

In these monthly evaluations, an important criterion of relative degree of muscle spasticity was the measurement, by means of the goniometer, of the angulation present at the ankles, knees and elbows when the respective "stretch reflex" was stimulated. The extent of muscle relaxation was considered "good" when the goniometer readings showed an improvement of more than 30 degrees, "fair" when it was between 15 and 30 degrees, and "poor" when it was less than 15 degrees.

Consideration was also given to functional improvement as evidenced by the patient's use of muscles and muscle groups—gait, flexion, extension, adduction and abduction, supination and pronation, circumduction, freedom of movement and coordination. And note was taken each month of the patient's progress in being freed of pathologic overflow muscle contractions (which are especially associated with athetosis).

After the data were recorded for this group of 72 children given carisoprodol, the author compared the results with a previous group of patients. These latter, numbering 51 patients, were closely similar to the carisoprodol-treated group in age and sex distribution and in types of disorder (See Table 2); therapy was identical for the two groups, excepting the use of carisoprodol on the study group.

RESULTS AND DISCUSSION

The response to this mode of treatment is summarized by type of case in Table 1. Taking the group of 72 patients as a whole, the results were judged satisfactory (good or fair) in 65 children, or 90%.

For comparison, it may be seen from Table 2 that a previous group of 51 patients, treated in very similar fashion but without carisoprodol, showed satisfactory (good or fair) results in 78% of cases.

TABLE 2

Results in 51 Patients—Treatment Not Including carisoprodol

Type of Case	Number of Patients	Results		
		Good	Fair	Poor
Spastic	25	8 (32%)	13 (52%)	4 (16%)
Rigidity	15	5 (33%)	7 (47%)	3 (20%)
Athetoid	10	2 (20%)	4 (40%)	4 (40%)
Ataxic	1	0	1 (100%)	0

Analysis of results is tabulated horizontally in each diagnostic category.

However, this percentile advantage of the group also treated with carisoprodol does not reveal the full benefits seen during therapy, which are not readily put into statistical data. In addition to the improvement in motor symptomatology, the effects of carisoprodol treatment could be seen in the fact that these children gained in poise, and were generally happier and more relaxed. As a result, there was an increase in attention span and a greater receptivity to school instruction and other educational activities. The children also tended to show less drooling during the course of treatment; they gained in ability to deal with braces or crutches and were better able to cooperate with the physiotherapist.

It should be pointed out that success in these conditions always requires patience in management, and the observations recorded in Table 3 serve to emphasize the importance of continuing the use of carisoprodol (as of any useful agent) in cerebral palsy for the period of time necessary in order to obtain optimal results.

TABLE 3

Progress of 72 carisoprodol-Treated Patients
During 14 Months of Clinical Study

Number of patents Evaluated	Time of Observation	Degree of Improvement (Cumulative)
14	At 2 mos.	30%
13	At 4 mos.	36%
7	At 6 mos.	45%
5	At 8 mos.	60%
8	At 10 mos.	75%
11	At 12 mos.	80%
14	At 14 mos.	90%
72		

From the author's experience in this study, there need be no qualms about untoward effects or problems arising from sustained use of carisoprodol. At the dosage level used—500 mg. total per day—side effects were practically nil. One child became a bit drowsy, confused and awkward in gait; the drug was discontinued and symptoms cleared in 24 hours. Another child became hyperactive; but this effect was eliminated by withdrawing the drug for 48 hours, after which therapy was resumed without further difficulty.

Because of its contribution to muscle relaxation and associated improvement in motor function, because of its helpful role also

in rendering the young patients better able to cope with the demands of social behavior generally, and because of its virtually complete freedom from side actions—carisoprodol is a welcome and valuable adjunct in the treatment of cerebral-palsied children.

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Brown, G. C. and Kendrick, P. L.: Serologic Response of Infants for a Multiple Vaccine for Simultaneous Immunization Against Diphtheria, Pertussis, Tetanus, and Poliomyelitis, in Relation to the Presence of Specific Maternal Antibody. (Amer. Jnl. Public Health 50:1529 Oct. 1960).

Forty-eight infants from 2 to 4 months of age were injected three times at intervals of one month with 0.5 ml of a multiple vaccine against diptheria, tetanus, pertussis, and poliomyelitis. Thirty-one of the children received an additional or booster dose from 6 to 12 months later. Serologic tests on prevaccination blood specimens revealed that very few of the infants had detectable antibodies to diptheria, tetanus, or pertussis, but the majority of them had poliomyelitis antibodies at this time. The response of the majority of the infants to the poliomyelitis components of the vaccine was definitely poorer than to the diptheria, tetanus and pertussis components. The lower serologic response to the poliomyelitis antigens was clearly associated with the presence of maternally-acquired passive antibodies in the infant's serum at the time of vaccination. The few children who had prevaccination antibodies to diptheria, tetanus, and pertussis also had poorer response than did those who were negative before vaccination. The suppressive effect of maternal antibodies affected not only the primary, but also the booster response to the several antigenic components; tetanus antibody production seemed to be least influenced. The significance of the findings is discussed.

Poison Control . . .

. . . ACCIDENTAL COBALT POISONING

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THE advice of the New York City Poison Control Center was recently requested on a cobalt poisoning which occurred in New Brunswick, New Jersey. A 19-month old male child obtained a container with a cobalt chloride solution and swallowed about one ounce of the contents. The father, who is a chemist, had brought the cobalt chloride salt home, and the patient's older brother prepared a solution to be used in making a weather indicator. Soon after the ingestion, the mother became aware of what had occurred and immediately induced vomiting four or five times. Within a half-hour following the last-induced vomiting, the child was admitted to a hospital emergency room where his stomach was lavaged. Shortly after admission, the lips and nail beds became cyanotic and the skin pale; the child became restless and drowsy. At this time, two hours after the first attempt at induced vomiting, the patient was unresponsive and died a few hours later in spite of the administration of intravenous fluids and supportive therapy.

A request for definitive information relating to the necropsy findings was addressed to Dr. William G. Wilentz, the Chief

* Assistant Commissioner for Maternal and Child Health, Department of Health, City of New York.
** Technical Director, Poison Control Center.

Medical Examiner of Middlesex County, New Jersey, who graciously supplied the following information:

"This child was admitted on an emergency basis because two hours before admission he had swallowed a mouthful of cobalt chloride. The mother made the child vomit four or five times by stimulation of the back of the throat. Shortly afterwards, the lips and nail beds turned blue and the skin became pale. The child then became restless and later drowsy. A day before admission he had swallowed 15 grains of acetylsalicylic acid and was immediately taken to Middlesex Hospital for gastric lavage. Apparently he had had no serious effect from this. On arrival in the emergency room, gastric lavage was again performed at this hospital. His past history was essentially negative except for one attack of spinal meningitis. Examination showed a well-developed and well-nourished, restless but somewhat drowsy infant. There was a hematoma present on the left upper lid. The pupils were regular and equal and reacted to light. The left drum was normal and the right drum was somewhat pinkish in color. The nose was clear; the lips were swollen and edematous. The tongue likewise was swollen and congested. The throat was congested. The neck was supple and no glands were felt. The chest was symmetrical. Rhonchi were present in both lungs. The heart was not enlarged and no murmurs were heard. The abdomen was soft and there were no masses or organs made out. No tenderness was present. External genitalia were normal. No gross external skeletal abnormalities were seen. The skin was pale and not appreciably cyanotic.

"Patient's course in the hospital was rapidly downhill. About one to one and a half hours following admission his respirations became labored and cyanosis supervened. The heart stopped beating very shortly thereafter. In spite of artificial respiration, epinephrine intramuscularly, oxygen and, finally, intracardiac adrenalin, the child could not be revived. He was pronounced dead approximately four and a half hours following entry to the hospital. Autopsy revealed very little evidence of the primary cause of death. The esophageal mucosa showed a few small bullae or blisters and the stomach showed a very definite thin layer of coagulative necrosis involving the inner one-third of the thickness of the mucosa. The mucosa and submucosa of the stomach were markedly congested. The blood vessels were dilated and filled with red blood cells. No abnormalities were noted in the lower intestinal tract including small intestine and colon. All of the other organs appeared to be entirely intact."

The toxicologic examination of the viscera, stomach contents and stools revealed the following:

Viscera (liver, kidney, spleen)—125 grams—cobalt (as Co), 0.0894 grams; stomach contents (11cc of a neutral—pH7—wine red liquid)—cobalt present; stool—cobalt present. The final clinical diagnosis was accidental poisoning—cobalt chloride. The final anatomical diagnosis was: 1. Cobalt chloride poisoning (clinical). 2. Hemorrhage, edema and congestion of gastric mucosa. 3. Coagulation necrosis, superficial, gastric mucosa. 4. Ecchymosis of left upper eyelid. 5. Otitis media, right, mild.

Microscopic examination revealed no unusual findings, except for the stomach and the brain which appeared damaged:

Stomach: The most prominent feature is marked congestion of both mucosa and submucosa with large dilated vascular channels in both layers packed with red blood cells. The superficial layer of the mucosa is also necrotic with complete vanishing of cell boundaries, nuclei, etc. This area of thin necrosis covering the surface involves about 1/3 of the mucosa. In one area of necrotic mucosa there is a deeply bluish-purple foreign body which may represent a cobalt crystal.

Brain: Except for edema of the brain, no unusual features were noted.

Another recent case of cobalt poisoning for which aid was requested from the New York City Poison Control Center, had a more felicitous outcome. A 3-year old child was left alone in the living room from which he wandered into the kitchen to get a drink of milk from the refrigerator. As he approached the refrigerator, his eyes were attracted to the small 29c. chemistry set which had been placed on top of it. With the aid of a chair he climbed up, obtained the set, and swallowed the contents of a glass tube in which his older sister had mixed cobalt and chloride. Though he apparently had no symptoms, the mother when told of the incident, called the Poison Control Center for advice. She was instructed to take the child either to a family physician or to a hospital emergency room. She hurriedly brought him to an emergency room where his stomach was lavaged. The patient was observed there for several hours and then sent home as improved. The public health nurse who visited the home reports the mother related this child is rather mischievous and very active and that she was unable to cope with his difficult behavior. The nurse advised well child supervision and also stressed

safety precautions with regard to the storage and handling of drugs and other potentially hazardous preparations, pointing out that chemistry sets should certainly be locked securely and kept out of reach of children.

We have previously reported a fatality in an adult, one of two alcoholics, who ingested a cobalt solution in the mistaken belief that it was wine.§

COBALT

Cobalt is essentially a trace element and a constituent of Vitamin B12. The average daily intake of cobalt in a normal American diet averages just about 5 micrograms. It is estimated that from 75 to 95 per cent of this amount is absorbed readily on the human intestines. It is chiefly excreted by the urine and, at times, by the bile and the feces. After oral ingestion, all but a very small fraction of it is excreted in six to eight days, about 35 per cent of this amount in the urine and the remainder in the feces.

In the past few years cobalt alone and in combination with iron has been used widely for the treatment of refractory anemias.

Toxicity of Cobalt: All cobalt preparations when used therapeutically can produce nausea, diarrhea, loss of appetite, flushing of the face and extremities, erythematous skin rashes, precordial pain, temporary nerve deafness, renal injury and thyroid enlargement. It has been reported that prolonged administration of cobalt chloride to anemic children may produce a goittrogenic action with hypothyroidism or thyroid hyperplasia. Cobalt has also been reported to produce a cobalt polycythemia with reticulocytosis, bone marrow hyperplasia and extramedullary erythropoietic activity, especially in the liver and spleen. The leucocytes are presumably not affected and it has been reported that the polycythemia does not occur when iron or copper are deficient or when the spleen has been removed. The mechanism by means of which cobalt causes polycythemia is obscure. It has been suggested, however, that the metal may inhibit certain respiratory enzymes in the bone marrow and the erythropoietic response is secondary to a local anoxia. While small doses of cobalt may produce a polycythemia, large amounts will depress erythrocyte production. It has also been reported that the inhalation of cobalt may cause

§ Jacobziner, Harold, M.D. and Raybin, Harry W., "Poisonings Associated with Bizarre Behavior," New York State Journal of Medicine, Vol. 60, No. 10, pp. 1634-1637, May 15, 1960.

nausea, vomiting, colicky pains, corrosion of the mucous membranes of the mouth and pharynx and moderate hemorrhage of the intestines. The continued handling of cobalt salts has also led to hypersensitivity and dermatitis.

While there is no specific antidote for the treatment of cobalt poisoning, EDTA has been suggested as a useful detoxicant in acute poisoning but BAL has apparently been of no value. The treatment is therefore chiefly symptomatic. It is emphasized that cobalt is a potentially toxic agent and should only be used when there is strong medical indication for its use. While cobalt may correct experimental anemias, especially those produced by benzene and turpentine, it has had very questionable effect in the treatment of clinical anemias. In anemias due to toxic inhibition of the erythropoietic function of the bone marrow, cobalt therapy is reported to be practically useless. It is therefore again strongly recommended that cobalt not be used indiscriminately in the treatment of anemias since it is a very hazardous substance.

Reports of the effectiveness of cobalt in the treatment of anemias are conflicting. Some claim it to be a powerful stimulent to the erythropoietic tissue of the bone marrow. In simple iron deficiency anemias, the accelerated erythropoiesis resulting from cobalt presumably creates a greater iron demand which may increase the absorption of iron.

Cobalt-iron therapy is said to be more effective in the treatment of nutritional anemia, anemia associated with prematurity and infection than iron therapy alone. The daily dosage for children under 5 years of age is 20-40 mg of cobalt chloride with ferrous sulfate, and for children over 5 years, 45-60 mg of cobalt chloride with ferrous sulfate. The only side effects noticed in a group of 50 children ranging between one month to 11 years in age were nausea, vomiting and loose stools in two children. The symptoms lasted for four days after therapy was discontinued. The side effects in eight patients with chronic monocytic monochromic anemia were mild abdominal distress and nausea and the symptoms abated with an increase in dosage. Hyperplasias of the thyroid with hypothyroidism have been reported in five negro children with sickle cell anemia from the prolonged use of cobalt. The thyroid deficiency however, disappeared within several weeks after the drug was discontinued.

Though cobalt does not affect the underlying disease, it is claimed by some to be beneficial in anemia secondary to chronic disease.

A group of pregnant women (20) who received cobalt chloride, 75-100 mg per day, experienced a decrease in hemoglobin level and hematocrit value in the same manner as the control group, whereas the groups receiving iron alone or iron and cobalt mixture did not experience such reductions. No toxic manifestations were noted in this group of pregnant women receiving cobalt either alone or in combination. All children born to these women were presumably normal. Good results have also been reported with cobalt chloride in the treatment of refractory anemias, while others claim it is of no value. Increases in hematocrit hemoglobin values and erythrocyte counts were said to be observed.

A few patients had gastrointestinal disturbances; one had a skin rash. The thyroid showed no enlargement in any of the patients studied. Cobalt is said to be useless in the treatment of anemia resulting from a toxic inhibition of the erythropoietic function of the bone marrow, either due to external causes such as from certain drugs or chemicals or from a chronic infection.

While many cobaltous preparations are available on the market and are recommended for the treatment of various anemias, it is the consensus of the most prominent authorities in hematology that cobalt chloride alone or in combination with iron is not more effective in the treatment of iron deficiency anemias than iron sulphate alone. It is also unwise to use cobaltous preparations in the treatment of refractory anemias associated with infections, since the rise in hemoglobin level which may be produced by cobalt in these cases is not sufficiently significant to warrant its use because of its potential toxic effects. Cobalt alone or in combination with iron should thus not be used therapeutically for the treatment of anemias.

Since cobalt chloride also has a wide distribution and availability to children as a constituent of chemistry sets, the fatality cited indicates that the use of cobalt in the home is associated with great hazards to children and also to adults. Cobalt is frequently used in chemical "tricks", such as secret writing and weather indicators. This would indicate more effective precautionary warning and labeling is warranted with regard to the dangers associated with the use and handling of this chemical, particularly by children.

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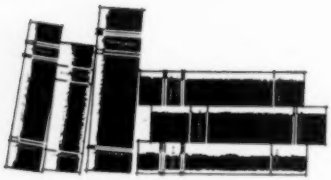
(This is the seventh of a series of papers by Dr. Jacobziner)



. . . Books

Edited by

MICHAEL A. BRESCIA, M.D.

PROTEIN AND AMINO ACID REQUIREMENTS IN EARLY LIFE. By L. Emmett Holt, Jr., M.D., Paul Gyorgy, M.D., Edward L. Pratt, M.D., Selma E. Snyderman, M.D., and William M. Wallace, M.D. New York University Press, 1960. $1.00.

Five prominent pediatricians, with the help of six other equally authoritative nutritionists have evaluated the available information on protein and amino acid requirements in early life.

Controversies have arisen concerning the interpretation of much of this data. This is acknowledged by the authors in a prefatory quote of Vilhalmur Stefansson. "There is probably no field of human thought in which sentiment and prejudice take the place of sound judgment and logical thinking so completely as dietetics." The authors have done a good job in pointing out these areas and the need for more research in them, without noticeable prejudice.

The minimal requirements of protein and amino acids, the optimal dietary amino acid pattern for health, the rapid maturation of the organism by generous protein intake and the effects of amino acid imbalance are some of the controversial issues which are discussed.

J. FREDERICK EAGLE, M.D.

REVIEW OF MEDICAL MICROBIOLOGY By Ernest Jawetz, Ph.D., M.D., Joseph L. Melnick, PhD., Edward A. Cedelberg, Ph.D., Fourth Edition, Pages 376, Card board cover, Lange Medical Publications, Los Altos, California, 1960, $5.

This text-book is written in order to make available for others, the practical knowledge which has been acquired in the field of microbiology in medicine. It is a brief, accurate, up-to-date presentation of those aspects of medical microbiology which are of particular significance in the fields of clinical infections and chemotherapy.

The review has been devoted to a discussion of the basic sciences which considers bacteriology, biochemistry, immunology, virology and antimicrobial chemotherapy. The practical results of the latter

are emphasized and the problems of immunity discussed. In general, details of technic and procedure as well controversial problems have been excluded.

There is clarity of expression and the subjects are treated in a most comprehensive manner, so as to make it a suitable text-book for medical students, residents, practicing physicians and internists. It is a work with positive scientific thought, and this reviewer recommends this text to all because of the recent important developments in the various basic sciences.

J. M. COVELLI, M.D.

DIFFERENTIALDIAGNOSE VON KRANKHEITSSUMPTOMEN BEI KINDERN UND JUGENDLICHEN. By Werner Catel, M.D. Volume 1, 3rd edition. Cloth Pp. 1051. 483 Illustrations. George Thieme, Stuttgart. 1961. DM220 $52.40.

This German text is the first of three volumes covering the differential diagnosis of diseases of children through adolescence. Since the first part of this trilogy already occupies over one thousand large pages, on completion this monumental contribution to pediatric literature may well be designated as an encyclopedia. As such, it will be of immense value to pediatricians confronted with difficult diagnostic problems.

This book is so organized as to enable the reader to rapidly review the various causes and manifestations of the subject under discussion, as for example, in the first chapter on inadequate growth.

The first volume includes discussion of Bones and Joints, Blood, Metabolism and the Endocrine System. Each chapter has introductory notes adequately covering the theoretical background of the subject essential for an understanding of the clinical picture. This is followed by a description and comparison of the various clinical manifestations.

The book is profusely illustrated with nearly 500 excellent photographs, some of them in color. There are also numerous tables.

The work shows every evidence of careful preparation. It is thoroughly documented and up to date. It is hoped that it will be translated into English. RUTH KESSLER, M.D.

DER LIQUOR CEREBROSPINALIS IM KINDESALTER By Dr. H. Schonenberg Chefarzt Der Kinderklinik Der Stadtischen Krankenalstalten Aachen with 42 illustrations. Georg Thieme Verlag, Stuttgart 1960. Lange Medical Publications $5.

This monograph on the spinal fluid is devoted specifically to the needs of the pediatrician and intends to fill a gap in the German pediatric literature. As the author mentions in the preface, an attempt is being made to outline the possibilities and limitations of the diagnostics of the spinal fluid based on modern concepts of anatomy, physiology and pathology. This object has been well accomplished. The book is divided into two parts. The first, general section contains chapters on the dynamics of the spinal fluid, tests of production and absorption, problems of the permeability of the various barriers, methods of electrophoresis, phase contrast and fluorescent microscopy of the spinal fluids cells as well as many other important tests and methods. The second, special part deals with changes observed in various inflammatory disorders of the central nervous system as well as brain tumors.

This book is well written and contains excellent illustrations. It offers a wealth of up-to-date information on every aspect of diagnostics by means of examination of the spinal fluid in children. It will be of value not only to the pediatrician, but also to the neurologist and the neuro-surgeon. MARFRED WEICHSEL, M.D.

EXPERT COMMITTEE ON POLIOMYELITIS, THIRD REPORT. World Health Organization: Technical Report Series, 1960, No. 203; 53 pages. Price: 3/6, $0.60, Sw. fr. 2.—. Also available in French and Spanish.

Since the last WHO Expert Committee on Poliomyelitis met in 1957, not only have inactivated poliovirus vaccines come into widespread use but live attenuated vaccines have been submitted to intensive study and, in some countries, have already been employed on a scale that could scarcely have been envisaged three years ago. These developments and the problems they raise are fully reviewed in the third report of the Expert Committee.

In most countries where inactivated vaccines have been widely used, the protection obtained has been of the order expected on the basis of controlled field trials. Manufacturing and testing problems appear to have diminished with increasing experience, but recent attempts to manufacture polyvalent vaccines

containing poliomyelitis antigen have raised some special problems. Experience with such multiple antigens is still too limited for their value to be assessed.

The safety of live poliomyelitis vaccines appears to have been satisfactorily demonstrated in a number of areas where they have been used on a large scale, and in all except two of these areas the incidence of poliomyelitis has fallen. It is still too soon, however, to evaluate the long-term effectiveness of live vaccines. Criteria for evaluating the safety and effectiveness of such vaccines are formulated in the report. In this connection, further research on virus markers and on the degree of viraemia produced by different strains is urgently needed. The capacity of the various strains to spread to contacts and in the community is also a matter needing investigation. The Committee proposed criteria for the selection of suitable strains and for grading the various strains of the three sets of vaccines in use. They also gave attention to the possible contamination of live poliovirus vaccines by simian viruses, and recommended the study of their pathogenicity and methods of differential inactivation.

The choice of inactivated or live virus vaccine for large-scale immunization programs will depend upon the epidemiological, social and economic circumstances of the country concerned. The Committee examined the advantages and disadvantages of the two types of vaccine from these aspects and suggested a number of considerations to be kept in mind by public health authorities when deciding which policy to adopt. Emphasis is laid on the importance of serological surveys and surveillance for the efficient conduct of immunization programs. Finally, attention is drawn to the increasing prevalence of other enterovirus infections (Coxsackie and ECHO viruses), which cause a wide range of clinical manifestations, sometimes resembling those of poliomyelitis. Continued research is needed in this field, especially to detect any increase in the severity of the clinical manifestations in special groups, for example, in newborn infants.

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2. Glaser, Jerome: *J. M. A. Georgia* 45:514, Dec., 1956.

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